ARSPHENAMINE (SALVARSAN) AND NEO-ARSPHENAMINE (NEO-SALVARSAN).

LICENSES ORDERED AND RULES AND STANDARDS PRESCRIBED FOR THEIR MANUFACTURE.

Upon the recommendation of the Public Health Service the rules and standards copied below were adopted by the Federal Trade Commission on March 4, 1918, for the control of establishments licensed for the manufacture and sale of arsphenamine and neo-arsphenamine.

So far licenses for the manufacture of these products have been issued to the following establishments:

Dermatological Research Laboratories, 1818 Lombard Street, Philadelphia, Pa.

Takamine Laboratory (Inc.), 120 Broadway, New York City.

Farbwerke-Hoechst Co., 122 Hudson Street, New York City.

Diarsenol Co. (Inc.), 475 Ellicott Square, Buffalo, N. Y.

RULES AND STANDARDS PRESCRIBED BY THE UNITED STATES PUBLIC HEALTH SERVICE FOR THE CONTROL OF LICENSEES FOR THE MANUFACTURE AND SALE OF ARSPHENAMINE.

(1) Except as provided in paragraph (3) hereof, only the abbreviated chemical term Arsphenamine immediately followed by the descriptive chemical name shall be used on packages to designate the preparation.

(2) Arsphenamine shall be offered for sale only in colorless glass ampules containing an atmosphere of an inert gas.

(3) Each package shall be plainly marked so as to show the license number, the lot number, the name of the preparation, the actual amount of arsphenamine in the container, and the name and address of the manufacturer, in the following manner:

License No. ———. Lot No. ———

This package contains ——— grams of Arsphenamine (hydrochloride of 3-diamino-4-dihydroxy-1-arsenobenzene), prepared under regulations issued by the Federal Trade Commission, and conforms with tests approved by the United States Public Health Service. Made by ———

No names of diseases or symptoms shall appear on any label or package.

The licensee shall use the name Arsphenamine, immediately followed by the extended scientific name of the article. The word Arsphenamine, when used upon labels attached to packages and cartons, shall be printed in 10-point Roman capitals. On ampules, 8-point Roman capitals may be used.

The licensee may, if he desires, use upon labels and packages his particular brand or trade name, provided that whenever any such brand or trade name is used it shall invariably be accompanied without intervening printed matter, with the name Arsphenamine and the extended scientific name of the article, as provided in the preceding paragraph.

(4) Before placing on the market, each lot shall be tested by the manufacturer as regards toxicity and arsenic content, and shall comply with the requirements of paragraphs (5) and (6) following. Detailed and permanent records of these tests shall be kept by the manufacturer and copies furnished to the commission immediately upon the completion of the tests.

(5) The total arsenic content of the air-dried drug shall not be below 29.5 nor above 31.57 per cent.

(6) The maximum tolerated dose for healthy albino rats shall not be below 60 milligrams per kilo body weight when a 2 per cent slightly alkaline solution of the drug in freshly glass-distilled water is injected intravenously at the rate of not more than 0.5 cubic centimeter per minute.

For each toxicity test a series of animals of not less than four shall be used, and at least 75 per cent of the animals injected with the maximum tolerated dose should survive 48 hours from the time of injection.

The rats shall not be anesthetized for the injection and shall weigh between 100 and 150 grams. Pregnant animals shall not be used.

(7) In addition to tests by the manufacturer, tests shall be made from time to time by the United States Public Health Service. For this purpose samples of each lot shall be forwarded by the manufacturer to the Hygienic Laboratory of the United States Public Health Service. The number of samples supplied shall be not less than 10 ampules from any lot, and from lots of over 1,000 ampules, 1 per cent shall be furnished. Each ampule forwarded shall contain at least 0.6 gram of Arsphenamine.

Officers of said service or of the Federal Trade Commission, when duly detailed, may enter establishments for the purpose of securing samples and conducting inspections.

(8) When lots have passed satisfactorily the prescribed tests, they may be offered for sale, but the right is reserved to require the withdrawal from the market of any lot designated by the Federal Trade Commission.

(9) Manufacturers shall retain 2 per cent of the ampules from each lot for a period of three months from the time the preparation is put in ampules; but the number retained need not exceed 10 ampules from each lot.

RULES AND STANDARDS PRESCRIBED BY THE UNITED STATES PUBLIC HEALTH SERVICE FOR THE CONTROL OF LICENSEES FOR THE MANUFACTURE AND SALE OF NEO-ARSPHENAMINE.

(1) Except as provided in paragraph (3) hereof, only the abbreviated chemical term Neo-Arsphenamine, immediately followed by the descriptive designation, shall be used on packages to designate the preparation.

(2) Neo-Arsphenamine shall be offered for sale only in colorless glass ampules containing an atmosphere of an inert gas.

(3) Each package shall be plainly marked so as to show the license number, the lot number, the name of the preparation, the actual amount of Neo-Arsphenamine in the container, and the name and address of the manufacturer in the following manner:

License No. ——. Lot No. ——.

This package contains —— grams of Neo-Arsphenamine (a compound prepared from Arsphenamine by means of formaldehyd-sulphoxylate), prepared under regulations issued by the Federal Trade Commission, and conforms with tests approved by the United States Public Health Service. Made by ——.

No name of diseases or symptoms shall appear on any label or package.

The licensee shall use the name Neo-Arsphenamine, immediately followed by the descriptive designation of the article. The word Neo-Arsphenamine, when used upon labels attached to packages and cartons, shall be printed in 10-point roman capitals. On ampules 8-point roman capitals may be used.

The licensee may, if he desires, use upon labels and packages his particular brand or trade name, provided that whenever any such brand or trade name is used it shall invariably be accompanied, without intervening printed matter, with the name Neo-Arsphenamine and the descriptive designation of the article, as provided in the preceding paragraph.

(4) Before placing on the market, each lot shall be tested by the manufacturer as regards toxicity and arsenic content, and shall comply with the requirements of paragraphs (5) and (6), following. Detailed and permanent records of these tests shall be kept by the manufacturer and copies furnished to the commission immediately upon the completion of the tests.

(5) The total arsenic content of the air-dried drug shall not be below 18 per cent nor above 20 per cent.

(6) The maximum tolerated dose for healthy albino rats shall not be below 90 milligrams per kilo body weight when a 2 per cent aqueous solution of the drug in freshly glass-distilled water is injected intravenously at the rate of not more than 0.5 cubic centimeter per minute.

For each toxicity test a series of animals of not less than four shall be used, and at least 75 per cent of the animals injected with the maximum tolerated dose should survive seven days from the time of injection.

The rats shall not be anesthetized for the injection and shall weigh between 100 and 150 grams. Pregnant animals shall not be used.

(7) In addition to tests by the manufacturer, tests shall be made from time to time by the United States Public Health Service. For this purpose samples of each lot shall be forwarded by the manufacturer to the hygienic laboratory of the United States Public Health Service. The number of samples supplied shall not be less than 10 ampules from any lot, and from lots of over 1,000 ampules 1 per cent shall be furnished. Each ampule forwarded shall contain at least 0.9 gram of Neo-Arsphenamine.

Officers of said service or of the Federal Trade Commission, when duly detailed, may enter establishments for the purpose of securing samples and conducting inspections.

(8) When lots have passed satisfactorily the prescribed tests, they may be offered for sale; but the right is reserved to require the withdrawal from the market of any lot designated by the Federal Trade Commission.

(9) Manufacturers shall retain 2 per cent of the ampules from each lot for a period of three months from the time the preparation is put in ampules, but the number retained need not exceed 10 ampules from any lot.